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Summary

The main focus of the current thesis was to investigate the long-term effectiveness of exercise therapy and the role of exercise adherence in patients with osteoarthritis (OA) of the hip or knee. It was hypothesized that the long-term effectiveness of exercise therapy declines after discharge and largely depends on the extent to which a person's behavior corresponds with agreed recommendations from the patient's physical therapist (exercise adherence). Furthermore, it was investigated whether a behavioral graded activity treatment can improve adherence and the long-term effectiveness in patients with OA of the hip and/or knee. For this purpose, data were used from a randomized controlled trial comparing behavioral graded activity (BGA) with usual exercise therapy (UC; exercise therapy according the Dutch guideline for physiotherapy) in patients with OA of the hip or knee.

In **chapter 1** the rationale for the presented research in this thesis was described. Osteoarthritis is a slowly progressive musculoskeletal disease causing pain, joint stiffness, deterioration of muscle weakness, instability of joints and threatening joint mobility, which often leads to moderate to severe impairments in activities, participation and a reduced quality of life. Patients with OA tend to avoid certain activities, because of pain during the performance of these activities. In the short-term, pain can be reduced by avoiding these activities. However, in the long-term, avoidance of activities can have physical consequences, such as loss of joint mobility, muscle strength and joint stability. Earlier research has shown that factors such as a loss of joint mobility, muscle strength and a lack of regular physical activity are important risk factors for functional decline in patients with OA of the hip or knee.

Several systematic reviews outline the effectiveness of exercise therapy in the OA population. These reviews conclude that there is strong evidence that exercise therapy has beneficial short-term effects on pain, physical function and patients' self perceived effect in patients with OA of hip and/or knee. Because OA of the hip and/or knee is a progressive disease and patients have to cope with their disease and its functional consequences for the rest of their lives, it is important that beneficial post-treatment results are sustained in the long term. However, most systematic reviews focused on short-term results, ignoring long-term effects. Therefore, a synthesis of the current evidence on

the long-term effectiveness of exercise therapy in patients with OA of the hip or knee was needed.

Several authors have suggested that the success of exercise therapy in patients with OA depends on the patients' level of adherence. Although it is well documented in the context of other chronic conditions, research to identify the extent to which adherence is a predictor of outcome in the management of OA remains limited. Previous studies in patients with OA predominantly focused on adherence within the period of treatment. For improving the long-term effectiveness of exercise therapy, it was hypothesized that adherence to recommended exercise behavior after the treatment period is an important predictor of patients outcome in the long-term. Furthermore, insight in predictors of exercise adherence is important, given the expectation that the effectiveness of exercise therapy, both within and after the treatment period, depends on patients level of adherence to the recommended exercise behavior.

To stimulate exercise adherence and a more physically active lifestyle post-treatment, it is suggested that exercise programs should become more functional and task-oriented, including additional booster sessions and strategies to improve exercise behavior and self-regulation skills. Veenhof et al. developed and evaluated an exercise program integrating operant behavioral principles, self-regulation principles and additional booster sessions called the 'behavioral graded activity' program. The behavioral graded activity treatment is an individually tailored exercise program in which patients' most problematic physical activities are gradually increased in a time contingent way. Furthermore, the intervention includes individually tailored exercises to improve impairments limiting the performance of these activities. The ultimate goal is integration of these exercises and activities in patients' daily living, so that patients get a more physically active lifestyle. In additional booster sessions patients are supported and stimulated to sustain their physically active lifestyle and integrate exercises and activities in their daily life. It was hypothesized that behavioral graded activity would result in better adherence to the recommended exercise behavior and consequently in better long-term

effectiveness than usual exercise therapy according the Dutch guideline in patients with osteoarthritis of the hip and/or knee.

The following research questions were formulated in the present thesis:

1. What is the long-term effectiveness of exercise therapy in patients with osteoarthritis of the hip and/or knee? (chapter 2)
2. What is the long-term effectiveness of behavioral graded activity on pain, physical function and patients global assessment compared with exercise therapy following the Dutch guideline for physiotherapy? (chapter 3)
3. What is the relationship between adherence and patients' outcome on pain, physical function and patients' self-perceived effect in exercise therapy treatment in patients with OA of the hip and/or knee? (chapter 4)
4. Does behavioral graded activity result in better exercise adherence and a higher level of physical activity than usual exercise therapy treatment (UC) in patients with OA of hip and/or knee? (chapter 5)
5. What are determinants of adherence to recommended exercises and/or activities within and after the period of treatment in therapeutic exercise therapy in patients with OA of the hip and/or knee? (chapter 6)

Chapter 2 presents the results of a systematic review in which the long-term effectiveness of exercise therapy in patients with osteoarthritis was investigated. An extensive literature search in PubMed, Embase, CINAHL, SCISEARCH, PEDro and the Cochrane Controlled Trial Register was carried out. Both randomized clinical trials and controlled clinical trials on the long-term effectiveness of exercise therapy were included. The follow-up assessments were at least 6 months after the treatment was ended. Methodological quality was independently assessed by two reviewers. Effect estimates were calculated and a best evidence synthesis was performed on basis of design, methodological quality, and statistical significance of findings.

Five high quality and six low quality randomized clinical trials were included. No evidence was found for the long-term effectiveness of exercise therapy on pain and physical function in patients with osteoarthritis of the

hip or knee. Long-term beneficial effectiveness was only found for patients' global assessment of effectiveness. Based on these results it was concluded that the positive post-treatment effects of exercise therapy on pain and physical function decline over time after discharge and finally disappear in the long-term. Some of the included studies investigated the value of additional booster sessions in the period between discharge and long-term follow-up. It was concluded that the use of additional booster sessions after the treatment period seems to have a positive influence on the maintenance of beneficial post-treatment effects on pain and physical function in the long term.

Chapter 3 presents the results of a follow-up study of a single blind randomized controlled trial investigating the long-term effectiveness of behavioral graded activity on pain, physical function and patients global assessment compared with exercise therapy following the Dutch guideline for physiotherapy. One hundred and forty-nine patients out of the 200 included were followed until 60 months follow-up. Primary outcome measures were pain, physical function, and patient global assessment. Furthermore, patient oriented physical function, physical performance, health care utilization and the number of joint replacement surgeries were assessed. Assessments took place at 3, 9, 15 and 60 months follow-up. Data were analyzed according to the intention-to-treat principle.

In patients with knee OA no differences between treatments were found on the short-, mid-long and long-term. In patients with hip OA significant differences in favor of behavioral graded activity were found at 3 months (pain and physical performance) and 9 months follow-up (pain, physical function, patients global assessment and patient oriented physical function). Furthermore, usual exercise therapy resulted in patients with hip OA in more joint replacement surgeries compared to behavioral graded activity. Based on these results it was concluded that although no significant differences between treatment groups were found in the long-term on pain and physical function, behavioral graded activity results in better short- and mid-long-term effects and a reduces risk for joint replacement surgery compared to usual exercise therapy in patients with hip OA.

Chapter 4 presents the results of a prospective observational follow-up study investigating the association between adherence to self-directed exercise within the prescribed physical therapy treatment period and after physical therapy discharge on patients outcome in individuals with osteoarthritis of the hip or knee. One hundred fifty patients with OA of the hip and/or knee receiving exercise therapy were followed 60 months. Data were obtained from a randomized controlled trial, with assessments at baseline, 3, 15, and 60 months follow-up. Exercise adherence was defined as the extent to which a person's behavior – doing home exercises, home activities and being more physically active – corresponds with agreed recommendations by the patient's physical therapist. The association between exercise adherence and patients' outcome on pain, physical function and self-perceived effect was examined using generalized estimating equations (GEE) analyses.

The results showed that better adherence to recommended home exercises as well as being more physically active improves the long-term effectiveness of exercise therapy in patients with osteoarthritis of the hip and/or knee. Both within and after the treatment period adherence was associated with better patients' outcome on pain, physical function, and self-perceived effect. Since exercise adherence declines over time, future research should focus on how exercise behavior can be stimulated and maintained in the long-term.

In **chapter 5** it was investigated if integration of behavioral graded activity principles including additional booster sessions can improve exercise adherence compared to usual exercise therapy. Secondary analyses were performed using the data of a cluster randomized clinical trial with concealed allocation and assessors blinded. The statistical analyses were carried out according to the intention-to-treat principle. Two hundred patients with hip and/or knee osteoarthritis were included. Exercise adherence and physical activity were measured with self-reported questionnaires. Assessments were conducted at 13 and 65 weeks follow-up.

In the short-term and long-term adherence to home exercises was significantly higher in the experimental group compared to control group. Furthermore, significantly more patients in the experimental group met the recommendations for the amount of moderate-vigorous intensity physical

activity compared to patients in the control group, both after 13 and 65 weeks follow-up. It was therefore concluded that behavioural graded activity results in better exercise adherence and a higher level of physical activity than usual physiotherapy treatment according the Dutch guideline for physiotherapy in patients with osteoarthritis of the hip or knee.

Because adherence to the recommended exercise behavior was found to be associated with better patient outcome within and after the treatment period, more insight in potential predictors of exercise adherence is important. The objective of **chapter 6** was to explore determinants of adherence to recommended home exercises and/or activities within and after the period of treatment in therapeutic exercise therapy in patients with osteoarthritis (OA) of the hip and/or knee. Data were obtained from a single blind randomized trial comparing behavioral graded activity (BGA) and usual exercise therapy (UC) according the Dutch guideline for physiotherapy in patients with OA of the knee or hip. Assessments took place at baseline, 3, and 15 months follow-up. The association between adherence and potential individual, psychological, intervention-related, and illness-related factors was investigated using univariate and multivariate logistic regression analyses.

The results showed that a more active coping strategy and a lower level of social support was associated with exercise adherence within the period of treatment. Exercise adherence after the treatment period was found to be associated with being adherent within the period of treatment. No significant predictors for activity adherence within the period of treatment were found. Activity adherence after the treatment period was associated with the prior experience with exercise therapy, a more passive pain coping strategy, and a higher improvement in physical functioning within the period of treatment. Based on these results it was concluded that psychological and treatment-related factors were associated with adherence within and after the treatment period. However, no consistent results were found for these factors across the different phases (within and after the treatment period) and between the different forms of adherence measured (exercise and activity adherence). Adherence to recommended exercises and activities seems not to depend on individual and illness related factors, both within and after the treatment period.

Chapter 7 discusses the main results of this thesis. Furthermore, implications for clinical physiotherapy practice, policy and future research are given.